What's New in the Treatment of Erythroblastosis

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THE Race-Fisher system of nomenclature of CDE-cde for the Rh-Hr system in the antigenic make-up simplifies the ever-increasing complexity of the problem of treating erythroblastosis and should be adopted universally. This system makes it possible to tell at first glance which persons will be sensitized, particularly in the rarer forms. The common single chromosome combinations are CDe, cde and cDE. If a woman with the genetic formula cde-cde (Rh-negative) is mated with a man whose genetic formula is CDe-CDe, (homozygous Rh-positive), the offspring will have the genetic formula of CDe-cde or always Rh-positive. If, however, this woman is mated with a man whose genetic formula is CDe-cde (a heterozygous Rh-positive), the offspring will have a 50-50 chance of being a cde-cde (Rh-negative). Formerly it was thought the Rh-negative lacked antigens, but we now know that they have three antigens known as c, d and e which are poor antigens and result in the rarer Hr factor. The anti-D serum has an 85 per cent specificity, the anti-c serum is important for the determination of heterozygosity, and anti-e serum for determining the 14 per cent who have a genetic formula, CDe-cDE.[6]

Until recently there was but one known method of treating erythroblastosis—multiple transfusions with Rh-negative blood, which was not adequate in all cases. Today a procedure known as exsanguination and replacement transfusion is available.

Exsanguination and replacement transfusion is indicated if there are severe signs and symptoms of erythroblastosis present at birth or if there is a family history indicative of chromosome incompatibility plus a strongly positive result of a Coombs' test,[5] conglutination test,[8] or gelatin test,[4] even though there is very little or no evidence of the disease at the time of birth. It remains to be seen whether exsanguination and replacement transfusion is advisable in cases in which there is strongly positive agglutination by one of the above methods but no history indicative of erythroblastosis and little or no evidence of the disease in the infant. There are several physicians in this country who feel that the procedure should be carried out in such circumstances, and yet in one of our recent cases only two transfusions were required. It must be emphasized that there are very mild cases of erythroblastosis fetalis in which the infant recovers without treatment, and some moderately severe cases in which multiple transfusions are effective.

The umbilical vein is used for transfusions done within 12 hours after delivery; for those carried out later, entry is made into the inferior vena cava by way of the great saphenous vein exposed in the upper thigh.[1] The use of the Diamond plastic catheter No. 18-19,[3] sterilized in Zephrin, for cannulizing these veins is the accepted procedure. Blood is withdrawn 20 cc. at a time and replaced with an equal amount of Rh-negative blood, the total of such exchanges varying from 250 to 500 cc. of blood, the amount depending usually on the severity of the disease. If anemia is present, 30 to 50 cc. more is given than is removed. Heparin, 10 mg. in normal saline, may be used as a rinse to keep the apparatus free of clots. As a final step 5 cc. of 10 per cent calcium gluconate is introduced through the cannula to counteract the excess citrate. It must be given well diluted, and better yet, in divided doses, to avoid heart block. Other procedures, such as withdrawal from the fontanel,[7] radial artery,[7] or femoral artery and introduction through the saphenous vein are used occasionally. Malony prefers to withdraw the blood from the umbilical vein and introduce the blood through the saphenous vein because in one case in which the blood was introduced through the umbilical vein, autopsy showed the mesenteric veins were thrombosed, resulting in a gangrenous bowel; and in another case free blood was found in the peritoneal cavity. Maintenance of oxygen supply and body temperature during the procedure is of utmost importance. Chemotherapy for four or five days thereafter is definitely indicated.

Induction of labor or Cesarean section for removal of the fetus prematurely in order to treat erythroblastosis should be used with reserve because the mortality rate from prematurity is greater than from the disease and actual benefit of the earlier treatment is very doubtful.

Beyond the measures now used, one other way of lowering the mortality rate from this disease is to have some program in each community whereby every pregnant woman may have the benefit of the Rh studies for a fixed price and those requiring further follow-up studies may have them without additional cost. In Pasadena such a program has proven very effective not only in lessening the financial burden of the Rh-negative mothers but in making it possible to alert the pediatrician for possible trouble.

The next step should be to prevent the development of this disease. We know that only one in every 25 of the Rh-negative wife and Rh-positive husband combinations have children with erythroblastosis and that in the presence of two antigens, antibodies will be produced for the stronger one. Therefore, it may be wise to give typhoid vaccine to Rh-negative sisters

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of Rh-negative mothers who have had infants with erythroblastosis, provided, of course, the blood of the sister's husband is such that erythroblastosis might be expected in the couple's offspring.

Bloxsom and Matthaei[2] have discovered a new factor, the anti-Rh antigen-antibody factor, which has been found to be present in high concentrations in Rh-negative mothers who, although having Rh-positive husbands, have normal offspring. As this factor has been found in Rh-negative male blood donors also, serum from these donors is being given to pregnant women in the hope of preventing or minimizing the disease in their children. Several other workers are using haptens, allergicil and normal saline for purposes of desensitization. Even if the anti-body titre can be reduced or the level maintained, it may not prove to be the answer, for frequently there is a marked discrepancy between the anti-body titre and the severity of the disease. It will be some time before work along this line can be fully evaluated and it will be interesting to follow the studies.

Another possibility for those having lost one or more infants and with husbands who are homozygous is artificial insemination with semen from an Rh-negative donor.

The publicity that has been given to the importance of erythroblastosis has caused undue alarm, particularly for young couples who have a hazardous Rh combination. It is the duty of physicians to explain to such persons that the disease occurs in only one infant in 25 whose parents have the combination, and that with present methods of treatment the mortality rate among infants who have the disease is about 10 per cent.

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QUESTIONS AND ANSWERS

Question: There is a question as to the indications for exsanguination transfusion. Let us take a child from the time of birth—whether or not he should have a transfusion.

DR. KIRCHDOERFER: If the child has all the signs and symptoms, particularly severe jaundice at birth, I think you go right ahead and assume he has erythroblastosis. If there is a family history of erythroblastosis and a positive reaction to agglutination tests or Coombs' test or other test, immediate exsanguination transfusion is probably indicated even though clinically the child does not seem to have the disease.

Question: Why give typhoid vaccine to mothers?

DR. KIRCHDOERFER: Weiner stated when you have two antigens present, the antibodies will be formed for the stronger antigens, and with that in mind it is believed that it disperses the others. That is just an idea that Weiner stated. I don't believe anybody ever tried it, or that there is anything on it—just a thought.